

Management of tricuspid regurgitation

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Abstract

Secondary tricuspid regurgitation is the most frequent type of tricuspid insufficiency in western countries. Its surgical treatment is still an object of debate both in terms of timing and surgical techniques. Until recently, the avoidance of surgery for tricuspid repair was commonly accepted in patients with less than severe secondary tricuspid regurgitation undergoing left-sided valve surgery. More recently, compelling evidence in favour of a more aggressive surgical approach in this setting has emerged. The surgical technique should be tailored to the stage of disease. Ring annuloplasty is more durable than suture annuloplasty and represents the method of choice in the presence of isolated annular dilatation. In patients in whom the dilatation of the tricuspid annulus is combined with significant leaflet tethering, annuloplasty alone is unlikely to be durable and additional procedures have been proposed in order to achieve a more durable repair. In this review, pathophysiology, surgical indications, techniques of repair and outcomes of secondary tricuspid regurgitation will be discussed. We will also focus on the challenging issue of significant tricuspid regurgitation occurring late after left-sided valve surgery. Finally, the current and future role of percutaneous tricuspid valve technologies will be briefly described.

Introduction

Tricuspid regurgitation due to primary valve lesions (organic) is nowadays a rather uncommon finding, particularly in western countries – where the most frequent type of tricuspid regurgitation is secondary tricuspid insufficiency [1]. Secondary (or functional) tricuspid regurgitation refers to tricuspid regurgitation occurring as a result of left-sided heart disease (LHD) or pulmonary hypertension in the absence of organic disease of the tricuspid valve. This definition, however, may be somewhat misleading since functional tricuspid regurgitation is not a truly functional entity, as it entails intrinsic anatomical abnormalities of the tricuspid apparatus, such as annular dilation and deformation.

The surgical treatment of secondary tricuspid regurgitation is still an object of debate both in terms of timing and surgical techniques. Until recently, the avoidance of surgery for tricuspid valve repair was easily accepted in

this setting on the basis of the incorrect concept that tricuspid regurgitation would disappear once the primary LHD had been treated [2]. This conservative approach still influences surgical practice today, and tricuspid valve repair for secondary tricuspid regurgitation still remains a rather uncommon procedure in many surgical centers. Over the past few years, many investigators have reported evidence in favour of a more aggressive surgical approach [3–5]. In addition, significant residual tricuspid regurgitation has been reported in 10 to 45% of patients after tricuspid valve repair with different techniques [6–10]. Consequently, interest has been growing in the physiopathology and treatment of secondary tricuspid regurgitation.

Pathophysiology of functional tricuspid regurgitation

The most common etiology of secondary tricuspid regurgitation is right ventricular dilation and dysfunction

from LHD [2,11]. Dilated cardiomyopathy and hypertensive pulmonary disease are less frequent causes of functional tricuspid regurgitation [2]. The pathophysiology of secondary tricuspid regurgitation may be divided into three phases [12]. In the first phase, initial dilation of the right ventricle results in tricuspid annulus dilation. Dilation of the tricuspid annulus occurs mainly in its posterior and anterior portions, corresponding to the free wall of the right ventricle, while the dilation of the septal segment is limited because of its close anatomical relationship with the fibrous skeleton of the heart. In this phase, tricuspid regurgitation may or may not be present, depending on the degree of annular dilation [3]. In the second phase, with progressive right ventricular and tricuspid annulus dilation, significant functional tricuspid regurgitation occurs because of the failure of leaflet coaptation [13]. Finally, with progressive right ventricular distortion and eccentricity, tethering of the leaflets occurs, in addition to tricuspid annulus dilation [14].

Conservative management

Conservative management of secondary tricuspid regurgitation includes optimization of right ventricular preload and afterload. Right ventricular overload may benefit from progressive use of diuretics and angiotensin-converting enzyme inhibitors. However, an excessive reduction in central venous pressure may result in worsening of tricuspid regurgitation severity [2]. The use of angiotensin-converting enzyme inhibitors is supported by evidence that chronic right ventricular pressure overload activates the renin-angiotensin-aldosterone system, which may contribute to fluid retention and ventricular remodelling.

Indications for tricuspid valve surgery in secondary tricuspid regurgitation

Severe secondary tricuspid regurgitation should be corrected at the same time as left-heart surgery is performed. Less than severe functional tricuspid regurgitation should be surgically corrected in cases of concomitant LHD requiring surgery in the presence of tricuspid annulus dilation. Indeed, in those circumstances, the diameter of the tricuspid annulus rather than the grade of regurgitation (which is highly subjective and variable) should be the criterion to indicate the need for concomitant tricuspid valve repair. Compelling data are now available showing that if the tricuspid annulus is dilated and is not corrected at the time of mitral valve surgery, it is very likely that significant late tricuspid regurgitation will occur. For that reason, the 2012 European Guidelines on Valvular Heart Disease recommend tricuspid annuloplasty even in the presence of only mild tricuspid regurgitation, whenever the tricuspid annulus is ≥ 40 mm or > 21 mm/m² on preoperative echocardiography [3,15-17]. This more aggressive treatment of tricuspid regurgitation has been

shown to positively affect patients' symptoms [3]. In cases of less than severe asymptomatic functional tricuspid regurgitation (and in the absence of LHD requiring surgery), conservative management and clinical follow-up should be carried out [17].

Surgical techniques and results

The principles of therapy for secondary tricuspid regurgitation include elimination of increased afterload to the right ventricle (by correction of LHD and optimization of left ventricular function) and correction of tricuspid annulus dilation and dysfunction, usually by tricuspid valve annuloplasty. If severe tricuspid valve tethering is present, the use of adjunctive surgical techniques to tricuspid annuloplasty (like enlargement of the anterior leaflet) or tricuspid valve replacement should be considered.

Tricuspid annular dilatation has always been the primary target of the surgical treatment of secondary tricuspid regurgitation and has usually been corrected by two main surgical methods: the suture annuloplasty and the ring annuloplasty.

With suture annuloplasty methods, annular size is reduced by using a continuous suture to purse string the annulus. Most suture annuloplasty techniques are modified versions of Kay bicuspidization [18] or De Vega annuloplasty, which consists of the plication of both the posterior and anterior annulus [19].

With rigid or semi-rigid prosthetic ring annuloplasty, the annulus is permanently fixed in a systolic position and the physiologic shape of the tricuspid valve is restored [20]. Flexible rings may be used as well, although they do decrease the size of the annulus but are unable to restore its normal morphology.

Neither suture nor ring annuloplasty consistently eliminate functional tricuspid regurgitation. The recurrence rate of significant tricuspid insufficiency after tricuspid annuloplasty is around 8–15% as soon as one month after surgery [9,21] and has been attributed to several factors, including the severity of preoperative tricuspid regurgitation [9,21,22], pulmonary hypertension [22], the presence of pacemakers [9], left ventricular dysfunction [9], increased left ventricular remodelling [21], severe tethering of the tricuspid leaflets and the use of suture rather than ring annuloplasty [9,10-29]. Most of the published studies, both randomized and observational, have demonstrated that ring annuloplasty repairs are more durable than suture annuloplasty, particularly in patients with severe tricuspid annular dilation or pulmonary hypertension [10, 23-29]. Among the different types of

prosthetic rings, the semi-rigid or rigid ones (either standard or 3-dimensional) have been associated with the best results and the least increase of recurrent tricuspid insufficiency over time. In two large series published by the Cleveland Clinic group, the degree of postoperative 3+ or 4+ tricuspid regurgitation remained stable over time with the Carpentier-Edwards ring (12% at 5 years and 17% at 8 years) and rose constantly, with the De Vega procedure reaching the overall rate of 24% at 5 years [21] and 33% at 8 years [9]. Besides being more durable, ring repairs also provide better long-term survival and event-free survival up to 15 years after surgery, compared to suture annuloplasty [25]. This is not surprising considering that moderate and severe tricuspid regurgitation is an important predictor of late mortality, independent of ventricular function and pulmonary artery pressure [28]. In contrast with the above reported data favouring ring procedures, there are a number of series reporting satisfactory results (both early and late) with both De Vega and Kay suture annuloplasty [22,30-33]. Most of these studies were published in the late 1980s and 1990s and have major limitations (including the use of freedom from reoperation as a marker of outcome and a very limited number of echocardiographic controls), with only a minority of the study patients, randomly selected, investigated at follow-up by color Doppler echocardiography.

In patients in whom the dilatation of the tricuspid annulus is combined with significant leaflet tethering, annuloplasty alone is unlikely to be durable [34]. Under those circumstances, it is suggested that additional procedures are used to achieve a more durable repair. In particular, the augmentation of the anterior leaflet with a pericardial patch and the "clover technique" have been successfully adopted in this context [35,36]. Although preliminary results with these approaches are encouraging, more data and longer follow-up are necessary to prove their effectiveness in the long-term and define their role as an alternative to tricuspid valve replacement in selected patients.

The challenge of late tricuspid regurgitation following previous mitral valve surgery

A particularly challenging problem is represented by the development of significant tricuspid regurgitation late after left-sided valve surgery. This late tricuspid regurgitation may occur from progression of seemingly insignificant tricuspid regurgitation (untreated at the time of initial mitral surgery) or from failure of a previously performed tricuspid annuloplasty.

In this subgroup with long-standing tricuspid insufficiency, surgical indications can be more challenging due to the presence of variable degrees of right ventricular dysfunction and pulmonary vascular disease. The dilatation of the

tricuspid annulus is usually associated with important tethering of the tricuspid leaflet, secondary to advanced remodeling of the right ventricle. In those circumstances, an isolated annuloplasty is often unable to restore durable competence of the tricuspid valve and most of those patients are still treated with tricuspid valve replacement, possibly on a beating heart and with complete preservation of the valvular and subvalvular apparatus.

Surgical treatment can be performed through a median sternotomy or a right anterolateral thoracotomy. The right thoracotomy represents a useful option in the reoperative setting, allowing avoidance of sternal re-entry and limitation of cardiac and grafts dissection. In those patients, hospital mortality is usually higher and late outcome is often disappointing. The predominant causes of death are low cardiac output syndrome and continuing heart failure. The major factors limiting survival are the preoperative condition of the right ventricle and the severity of secondary renal and hepatic impairment [9,37]. Typically, patients with severe tricuspid regurgitation after mitral valve surgery are managed medically for a long time and are referred to surgery only when they develop severe incapacitating symptoms of right heart failure and organ dysfunction. At this stage, surgery is associated with high mortality and morbidity. This perpetuates the notion that surgical treatment of tricuspid regurgitation, following left-sided valve surgery, is a high-risk procedure, which further delays the surgical referral and increases the reluctance to operate on these patients. Since late surgical referral explains most of the unfavourable outcomes reported, the only way to interrupt this vicious circle is by earlier surgical indication. Patients submitted to left-sided valve surgery should be closely followed up and, if significant tricuspid regurgitation develops, early surgical treatment should be recommended before the occurrence of right ventricular dysfunction. This attitude is certainly appropriate and has already been implemented, at least in part, in the new 2012 European Guidelines on the management of Valvular Heart Disease [17]. The previously recommended "symptoms-guided" surgical referral has been significantly modified in the new guidelines, which state that surgical intervention should now be considered in patients with severe primary tricuspid regurgitation or persistent/recurrent severe tricuspid regurgitation after left-sided valve surgery if signs of progressive right ventricular dilatation or dysfunction are detected, even in asymptomatic patients. Delaying surgery in the above mentioned circumstances is likely to result in irreversible right ventricular damage, organ failure, and poor results. Of course, besides the degree of right ventricular dysfunction, the decision-making process in managing these patients should also take into account the presence of left-sided valve dysfunction, left ventricular dysfunction and pulmonary vascular disease [17].

Besides conventional echocardiography, tissue Doppler imaging, 3D echocardiography and magnetic resonance (which is probably the best method to assess right ventricular function) might prove useful in the future to better define the ideal timing of surgery. Whenever surgical referral occurs late, careful preoperative risk stratification by the "Heart team" is mandatory in order to exclude those patients who are unlikely to survive or to benefit from tricuspid valve surgery.

Interventional cardiology perspectives

Percutaneous procedures may be an attractive alternative to surgery for patients deemed to be high-risk surgical candidates. Whereas over the past few years the development and clinical use of percutaneous approaches to the aortic valve and mitral valve have been widespread, few data are available about the feasibility and efficacy of the percutaneous tricuspid valve approach. Some of the concepts that have been developed for the percutaneous treatment of mitral regurgitation may be adapted to percutaneous repair of the tricuspid valve (percutaneous annuloplasty, edge-to-edge repair) [38,39].

Different new devices are currently under preclinical development: the Millipede system (Millipede, LLC, Ann Arbor, Michigan) involves the placement of a tricuspid annular ring with an attachment system *via* either minimally invasive surgical or percutaneous methods to restore the native tricuspid annular shape and diameter. It is repositionable and retrievable before deployment.

The feasibility of the implantation of a valved stent into the tricuspid position has been described using *in vivo* animal models [40]. Iino *et al.* [41] reported the feasibility of off-pump transapical tricuspid valved stent implantation in an acute animal model, using a novel valved stent with a self-expandable, superabsorbent polymer to reduce paravalvular leakage. Beating-heart transcatheter tricuspid valve implantation to treat a degenerated bioprosthesis in tricuspid position through direct transatrial or transjugular access has been reported [42,43]. An alternative approach to percutaneous treatment of tricuspid valve is the implantation of separate valves in the superior vena cava and inferior vena cava to prevent damage to the liver and other organs [44].

The transcatheter implantation of a bioprosthetic in the tricuspid position presents challenging issues, such as the large dimension of the tricuspid annulus, the slow flow of the right-heart side, and the trabeculated structure of the right ventricle. With regard to access, the angulation of the annulus in relation to the superior vena cava and inferior vena cava requires careful consideration. Alternatively, transapical right ventricle access may be used, but the right

ventricular wall is thinner than the left ventricular wall, and multiple chordae may prevent the advance of the delivery system [38,39]. Therefore, several issues need to be addressed before we include percutaneous tricuspid valve technologies in our armamentarium. These might be useful in the future for selected tricuspid regurgitation patients who are at high risk for open-heart surgery.

Conclusions

The surgical treatment of secondary tricuspid regurgitation is still an object of debate. Severe secondary tricuspid regurgitation should always be corrected at the time of left-heart surgery. In less than severe functional tricuspid regurgitation, the diameter of the tricuspid annulus (rather than the grade of regurgitation) should be the criterion to indicate the need for concomitant tricuspid valve repair. If the tricuspid annulus is dilated, tricuspid annuloplasty should be performed during left-sided valve surgery. A ring annuloplasty represents a more durable solution than suture annuloplasty. When the dilatation of the tricuspid annulus is combined with significant leaflet tethering, adjunctive surgical techniques should be added to tricuspid annuloplasty, or valve replacement should be performed. A more aggressive management of secondary tricuspid regurgitation such as this could hopefully decrease the occurrence of late tricuspid regurgitation following previous mitral valve surgery. This remains a challenging problem whose surgical treatment is associated with high hospital mortality and poor postoperative outcome.

In patients with persistent or recurrent tricuspid regurgitation after left-sided surgery, earlier intervention should be recommended before the occurrence of right ventricular dysfunction. If surgical referral occurs late, the risk/benefit ratio of surgery should be discussed with a "Heart team" approach.

In the future, percutaneous tricuspid valve technologies might become an alternative option to treat selected tricuspid regurgitation patients with high surgical risk.

Abbreviations

LHD, left-sided heart disease.

Disclosures

The authors declare that they have no disclosures.

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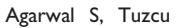
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